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L4 and l3	16

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**DATE: Thursday, February 21, 2002** [Printable Copy](#) [Create Case](#)

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<u>L5</u>	L4 and l3	16	<u>L5</u>
<u>L4</u>	toxicity	64321	<u>L4</u>
<u>L3</u>	L2 and l1	63	<u>L3</u>
<u>L2</u>	(gene or protein) near8 expression	32678	<u>L2</u>
<u>L1</u>	embryoid adj body	71	<u>L1</u>

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1. Document ID: US 20020019046 A1

L5: Entry 1 of 16

File: PGPB

Feb 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020019046

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020019046 A1

TITLE: Direct differentiation of human pluripotent stem cells and characterization of differentiated cells

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Draw. Desc](#) | [Image](#)

2. Document ID: US 20020009743 A1

L5: Entry 2 of 16

File: PGPB

Jan 24, 2002

PGPUB-DOCUMENT-NUMBER: 20020009743

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020009743 A1

TITLE: Neural progenitor cell populations

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Draw. Desc](#) | [Image](#)

3. Document ID: US 20010039006 A1

L5: Entry 3 of 16

File: PGPB

Nov 8, 2001

PGPUB-DOCUMENT-NUMBER: 20010039006

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010039006 A1

TITLE: Toxicity typing using embryoid bodies[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Draw. Desc](#) | [Image](#)

4. Document ID: US 6342356 B1

L5: Entry 4 of 16

File: USPT

Jan 29, 2002

US-PAT-NO: 6342356

DOCUMENT-IDENTIFIER: US 6342356 B1

TITLE: Methods and reagents for identifying synthetic genetic elements

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#)[KMC](#) | [Draw. Desc](#) | [Image](#)

5. Document ID: US 6156733 A

L5: Entry 5 of 16

File: USPT

Dec 5, 2000

US-PAT-NO: 6156733

DOCUMENT-IDENTIFIER: US 6156733 A

TITLE: Use of leukemia inhibitory factor and endothelin antagonists

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KMPC	Draw Desc	Image
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 6. Document ID: US 6117650 A

L5: Entry 6 of 16

File: USPT

Sep 12, 2000

US-PAT-NO: 6117650

DOCUMENT-IDENTIFIER: US 6117650 A

TITLE: Assay for cardiac hypertrophy

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KMPC	Draw Desc	Image
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 7. Document ID: US 6007993 A

L5: Entry 7 of 16

File: USPT

Dec 28, 1999

US-PAT-NO: 6007993

DOCUMENT-IDENTIFIER: US 6007993 A

TITLE: In vitro test for embryotoxic and teratogenic agents using differentiation-dependent reporter expression in pluripotent rodent embryonic cells

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KMPC	Draw Desc	Image
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 8. Document ID: US 5837241 A

L5: Entry 8 of 16

File: USPT

Nov 17, 1998

US-PAT-NO: 5837241

DOCUMENT-IDENTIFIER: US 5837241 A

TITLE: Method of treating heart failure using leukemia inhibitory factor antagonists optionally with endothelin antagonists

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KMPC	Draw Desc	Image
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 9. Document ID: US 5723585 A

L5: Entry 9 of 16

File: USPT

Mar 3, 1998

US-PAT-NO: 5723585

DOCUMENT-IDENTIFIER: US 5723585 A

TITLE: Method of purifying cardiac hypertrophy factor

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KMPC	Draw Desc	Image
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10. Document ID: US 5679545 A

L5: Entry 10 of 16

File: USPT

Oct 21, 1997

US-PAT-NO: 5679545

DOCUMENT-IDENTIFIER: US 5679545 A

TITLE: Gene encoding cardiac hypertrophy factor

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#)[KMC](#) [Draw Desc](#) [Image](#) 11. Document ID: US 5627073 A

L5: Entry 11 of 16

File: USPT

May 6, 1997

US-PAT-NO: 5627073

DOCUMENT-IDENTIFIER: US 5627073 A

TITLE: Hybridomas producing antibodies to cardiac hypertrophy factor

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#)[KMC](#) [Draw Desc](#) [Image](#) 12. Document ID: US 5624806 A

L5: Entry 12 of 16

File: USPT

Apr 29, 1997

US-PAT-NO: 5624806

DOCUMENT-IDENTIFIER: US 5624806 A

TITLE: Antibodies to cardiac hypertrophy factor and uses thereof

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#)[KMC](#) [Draw Desc](#) [Image](#) 13. Document ID: US 5573762 A

L5: Entry 13 of 16

File: USPT

Nov 12, 1996

US-PAT-NO: 5573762

DOCUMENT-IDENTIFIER: US 5573762 A

TITLE: Use of leukemia inhibitory factor specific antibodies and endothelin antagonists for treatment of cardiac hypertrophy

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#)[KMC](#) [Draw Desc](#) [Image](#) 14. Document ID: US 5571893 A

L5: Entry 14 of 16

File: USPT

Nov 5, 1996

US-PAT-NO: 5571893

DOCUMENT-IDENTIFIER: US 5571893 A

TITLE: Cardiac hypertrophy factor

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Sequences](#) [Attachments](#)[KMC](#) [Draw Desc](#) [Image](#)

L5: Entry 15 of 16

File: USPT

Nov 5, 1996

US-PAT-NO: 5571675

DOCUMENT-IDENTIFIER: US 5571675 A

TITLE: Detection and amplification of cardiotrophin-1(cardiac hypertrophy factor)

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [KMC](#) | [Draw Desc](#) | [Image](#) 16. Document ID: US 5534615 A

L5: Entry 16 of 16

File: USPT

Jul 9, 1996

US-PAT-NO: 5534615

DOCUMENT-IDENTIFIER: US 5534615 A

TITLE: Cardiac hypertrophy factor and uses therefor

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [KMC](#) | [Draw Desc](#) | [Image](#)[Generate Collection](#)[Print](#)

Terms	Documents
L4 and l3	16

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=> d his

(FILE 'HOME' ENTERED AT 17:47:12 ON 21 FEB 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 17:47:23 ON 21 FEB 2002

L1 1650 S EMBRYOID(W) BODY  
L2 693 S (CHEMICAL OR TEST) (W) COMPOUND(10A) TOXICITY  
L3 0 S L1 AND L2  
L4 29945 S (CHEMICAL OR TEST) (W) COMPOUND  
L5 4 S L1 AND L4  
L6 1 DUP REM L5 (3 DUPLICATES REMOVED)  
L7 1066502 S (GENE OR PROTEIN) (8A) EXPRESSION  
L8 571 S L1 AND L7  
L9 6 S L8 AND TOXICITY  
L10 252 DUP REM L8 (319 DUPLICATES REMOVED)  
L11 3 DUP REM L9 (3 DUPLICATES REMOVED)

=> d au ti so ab 16

L6 ANSWER 1 OF 1 MEDLINE DUPLICATE 1  
AU Schmidt M M; Guan K; Wobus A M  
TI Lithium influences differentiation and tissue-specific gene expression of mouse embryonic stem (ES) cells in vitro.  
SO INTERNATIONAL JOURNAL OF DEVELOPMENTAL BIOLOGY, (2001 Apr) 45 (2) 421-9.

Journal code: AV3; 8917470. ISSN: 0214-6282.  
AB The effects of lithium chloride (LiCl) on differentiation of mouse embryonic stem (ES) cells were investigated in order to evaluate the ES cell test (EST) used in a European Union validation study for screening of embryotoxic agents in vitro. We show that LiCl inhibited concentration-dependently the differentiation of ES cells into cardiac and myogenic cells. Whereas the inhibition of cardiac differentiation by high concentrations of LiCl was obvious at day 5 + 5, decreased skeletal muscle cell differentiation was observed only at day 5 + 8. Semi-quantitative RT-PCR analyses revealed significantly lower levels of mRNA encoding cardiac-specific alpha-myosin heavy chain and skeletal muscle-specific myoD. By morphological investigation, an influence of lithium on neuronal differentiation was not evident. However, mRNA levels of genes encoding synaptophysin and the 160 kDa neurofilament protein were increased by high LiCl concentrations, whereas mRNA levels of mash-1 and Engrailed-1 were decreased, suggesting a specific influence of lithium on neuronal differentiation. Furthermore, LiCl treatment resulted in a slight, but non-significant increase of beta-catenin levels in ES cell-derived **embryoid bodies**. Our results demonstrate that the ES cell test, EST may be suitable to detect inhibitory effects of **test compounds** especially on cardiac differentiation, whereas effects on neuronal cells would not be detected. Therefore, we propose that morphological analyses of cardiac differentiation alone are insufficient to detect embryotoxic effects. The assay of other cell lineages at different developmental stages, and expression analyses of tissue-specific genes should also be employed.

=> d au ti so ab 1-3 l11

L11 ANSWER 1 OF 3 MEDLINE  
AU Schmidt M M; Guan K; Wobus A M  
TI Lithium influences differentiation and tissue-specific gene expression of mouse embryonic stem (ES) cells in vitro.  
SO INTERNATIONAL JOURNAL OF DEVELOPMENTAL BIOLOGY, (2001 Apr) 45 (2) 421-9.

Journal code: AV3; 8917470. ISSN: 0214-6282.  
AB The effects of lithium chloride (LiCl) on differentiation of mouse embryonic stem (ES) cells were investigated in order to evaluate the ES cell test (EST) used in a European Union validation study for screening of embryotoxic agents in vitro. We show that LiCl inhibited concentration-dependently the differentiation of ES cells into cardiac and myogenic cells. Whereas the inhibition of cardiac differentiation by high concentrations of LiCl was obvious at day 5 + 5, decreased skeletal muscle cell differentiation was observed only at day 5 + 8. Semi-quantitative RT-PCR analyses revealed significantly lower levels of mRNA encoding cardiac-specific alpha-myosin heavy chain and skeletal muscle-specific myoD. By morphological investigation, an influence of lithium on neuronal differentiation was not evident. However, mRNA levels of genes encoding synaptophysin and the 160 kDa neurofilament protein were increased by high LiCl concentrations, whereas mRNA levels of mash-1 and Engrailed-1 were decreased, suggesting a specific influence of lithium on neuronal differentiation. Furthermore, LiCl treatment resulted in a slight, but non-significant increase of beta-catenin levels in ES cell-derived **embryoid bodies**. Our results demonstrate that the ES cell test, EST may be suitable to detect inhibitory effects of test compounds especially on cardiac differentiation, whereas effects on neuronal cells would not be detected. Therefore, we propose that morphological analyses of cardiac differentiation alone are insufficient to detect embryotoxic effects. The assay of other cell lineages at different developmental stages, and **expression** analyses of tissue-specific **genes** should also be employed.

L11 ANSWER 2 OF 3 MEDLINE DUPLICATE 1  
AU Bremer S; Worth A P; Paparella M; Bigot K; Kolossov E; Fleischmann B K; Hescheler J; Balls M  
TI Establishment of an in vitro reporter gene assay for developmental cardiac toxicity.  
SO TOXICOLOGY IN VITRO, (2001 Jun) 15 (3) 215-23.  
Journal code: DNS; 8712158. ISSN: 0887-2333.  
AB This study is based on the unique potential of pluripotent embryonic stem (ES) cells to differentiate in vitro into **embryoid bodies** containing cell lineages representative of most cell types found in the mammalian fetus. However, the use of wild type ES cells as an in vitro assay for embryotoxicological studies is complicated by the simultaneous development of various cellular phenotypes. This prevents a quantitative assessment of drug effects on one specific cell type. Here we report the effects of 15 chemicals on cardiac differentiation as determined by various specific toxicological endpoints such as morphological inspection (contractile activity), quantitative mRNA analysis and cardiac-specific **expression** of green fluorescent protein (GFP), used as a quantitative reporter. The data from the

different endpoints have been subjected to a statistical analysis, and a preliminary prediction model is proposed. The results demonstrate that genetically-engineered ES cells could provide a valuable tool for estimating the developmental cardiotoxic potential of compounds *in vitro* and form the basis for automated analysis in a high-throughput system.

L11 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS  
IN Snodgrass, H. Ralph  
TI **Toxicity typing using embryoid bodies**  
SO PCT Int. Appl., 56 pp.  
CODEN: PIXXD2  
AB This invention provides methods and systems for identifying and typing **toxicity** of chem. compns., as well as for screening new compns. for **toxicity**. The invention involves detecting alterations in **gene or protein expression** and hence establishing mol. profiles in isolated mammalian **embryoid bodies** contacted with various chem. compns. of known and unknown **toxicities**, and correlating the mol. profiles with **toxicities** of the chem. compns.

=> d bib 3 111

L11 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS  
AN 2000:402043 CAPLUS  
DN 133:26835  
TI **Toxicity typing using embryoid bodies**  
IN Snodgrass, H. Ralph  
PA Vistagen, Inc., USA  
SO PCT Int. Appl., 56 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000034525	A1	20000615	WO 1999-US29384	19991209
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP	1137809	A1	20011004	EP 1999-963069	19991209
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
	US 2001039006	A1	20011108	US 2001-864621	20010523
PRAI	US 1998-111640	P	19981209		
	US 1999-457931	A	19991208		
	WO 1999-US29384	W	19991209		

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

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